Summary of Safety and Effectiveness Data

I. General Information

Device Generic Name:	Vascular hemostasis device
Device Trade Name:	Vascular Solutions D-Stat® Flowable Hemostat
Applicant's Name and Address:	Vascular Solutions, Inc. 6464 Sycamore Court Minneapolis, MN 55369
Premarket Approval Application (PMA) Number:	P990037/S24
Date of Panel Recommendation:	None
Date of Notice of Approval to Applicant:	December 22, 2006

The original PMA application, P990037, for the Vascular Solutions Duett Sealing Device was approved on June 22, 2000 for the indication of sealing femoral arterial puncture sites and reducing time to hemostasis and ambulation in patients who have undergone diagnostic or interventional endovascular procedures using a 5F-9F introducer sheath with an overall length not exceeding 15.2 cm. The sponsor submitted this supplement to expand the clinical indications. The updated clinical data to support the expanded indication for use in the pre-pectoral pocket of high-risk anti-coagulated patients undergoing implantation of a pulse generator are presented in this summary. The pre-clinical results were presented in the original PMA application. Note that D-Stat Flowable uses the formulation of thrombin, collagen and diluent of the 2nd generation Duett product (now called Diagnostic Duett) approved in November 2001 as P990037/S001. The D-Stat Flowable was approved in May 2002 in P990037/S008. Neither P990037/S001 nor P990037/S008 required updates to the SSED. For more information on the data which supported the original indication, the summary of safety and effectiveness data to the original PMA should be referenced. Written requests for copies of the summary of safety and effectiveness data can be obtained from the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Drive, rm. 1-23, Rockville, MD 20857 under docket #00M-1390 and may be found on the FDA CDRH Internet Homepage located at http://www.fda.gov/cdrh/pmapage.html.

II. Indications for Use

D-Stat Flowable is indicated for use in high-risk anti-coagulated patients undergoing implantation of a pulse generator (e.g., pacemaker or ICD to reduce the frequency of clinically relevant hematoma formation in the prepectoral pocket. High-risk patients are defined as those whose anti-coagulation regimens will resume within 24 hours of implant. Clinically relevant hematomas are defined as those that result in an alteration in the standard of care resultant of hematoma formation including alteration (i.e. suspension or discontinuation) of the anticoagulant therapy regimen (Heparin, LMWH, Warfarin, or Clopidogrel), application of a compression bandage and evacuation of the hematoma.

III. Contraindications

D-Stat is contraindicated in persons with known sensitivity to bovine-derived materials.

IV. Warnings and Precautions

The warnings and precautions can be found in the D-Stat Flowable Hemostat labeling.

V. Device Description

The D-Stat Flowable Hemostat is comprised of a three-part procoagulant mixture consisting of collagen, thrombin in a buffered diluent. The D-Stat Flowable Hemostat achieves its principal intended action (hemostasis) by creating a physical barrier to blood flow and establishes an environment in which a natural blood clot can build and form a physical barrier to bleeding. The surface properties of the suspended collagen facilitate hemostasis reactions by enhancing the surface-activated clotting cascaded through enzymatic cleavage and conversion of fibrinogen to fibrin. The device also contains several delivery tools and mixing accessories. The device is sterilized with ethylene oxide.

A. Materials and Configuration

Each Vascular Solutions D-Stat flowable hemostat (D-Stat) includes the following components:

- Thrombin vial (5,000 units)
- Collagen (200 mg), contained in 10 ml syringe with attached mixing luer
- Diluent vial (5 ml)
- Mixing accessories (10 ml syringe and needleless, non-coring vial access device)
- Applicator tips: (1 small bore tip, (1) 20-gauge 2.75" needle)

The thrombin is a protein substance produced through a conversion reaction in which prothrombin of bovine origin is activated by tissue thromboplastin of bovine-origin in the presence of calcium chloride. It is supplied as a sterile powder that has been freeze-dried in the final container. Also contained in the thrombin vial are mannitol and sodium chloride. Mannitol is included to make the dried product friable and more readily soluble. The material contains no preservatives and has been chromatographically purified. Thrombin requires no intermediate physiological agent for its reaction. It converts fibrinogen directly to fibrin.

The collagen is a soft, white, pliable, absorbent hemostatic agent derived from purified bovine deep flexor tendon. It is prepared in a loose fibrous form. Collagen attracts platelets that adhere to the fibrils and undergo the release phenomenon to trigger aggregation of platelets into thrombi in the interstices of the fibrous mass. The collagen provides a three-dimensional matrix for additional strengthening of the clot. The effect on platelet adhesion and aggregation is not inhibited by heparin in vitro.

The diluent is a sterile solution of calcium chloride and water, buffered with tromethamine (TRIS). Using the mixing accessories, both the thrombin and collagen are reconstituted with the diluent prior to use. The hemostat is delivered to the intended treatment site using the provided applicator tips. Hemostasis is achieved by the physiological coagulation-inducing properties of the D-Stat. The D-Stat is biocompatible, non-pyrogenic, and intended to be left *in situ*.

B. Principals of Use

As early as 3 hours prior to use, the D-Stat procoagulant may be prepared following the mixing steps outlined in the *Instructions for Use*. Following the creation of the prepectoral pocket, subsequent antibiotic flush and selection of the desired applicator tip for D-Stat delivery, the skin flap is lifted, and a 5 ml bolus of D-Stat is delivered directly into the pocket. Light manual compression is then applied directly over the pocket for 2 – 3 minutes as necessary. The site is observed for bleeding within the pocket. If hemostasis is achieved, the pulse generator device function is assessed per the manufacturer's instructions and subsequently placed within the prepectoral pocket per the institution's protocol. Slight manual compression may be applied for 2 – 3 minutes as necessary. The pocket is closed in accordance with the institution's standard of care. Following pocket closure, a maximum of 1 ml of D-Stat may be applied as needed to control oozing at the suture line. An appropriate dressing is applied to the treated site. Follow-up observation and care is administered in accordance with the institution's protocol.

In the event hemostasis of the pocket is not achieved following the initial 2 – 3 minutes of compression or if bleeding continues, a second package of D-Stat may be prepared and administered, delivering a subsequent bolus of no greater than 6 ml. Light manual compression is applied for 2 – 3 minutes as necessary. The wound is assessed for hemostasis per the direction above. If hemostasis is achieved the pulse generator is evaluated according to the manufacturer's instructions and the generator is placed within the pocket. With closure of the pocket obtained as previously referenced, a 1 ml of D-Stat may be applied as needed to control oozing at the suture line. If persistent bleeding occurs, do not apply additional D-Stat. Rather, electrocautery, standard manual compression, or the institution's standard of care for persistent bleeding of the prepectoral pocket should be implemented. Subsequent management and care of the wound is performed per the institution's protocol.

VI. Alternative Practices and Procedures

Alternative methods to obtain hemostasis in the prepectoral pocket during implantation of a pulse generator include standard compression, electrocautery, and/or use of untreated cotton pledgets.

VII. Marketing History

D-Stat was approved for commercial distribution in the United States January 18, 2002 and is commercially marketed under PMA P990037 and 510(k) K012293. It has been marketed since that time for the local management and control of bleeding from vascular access sites and percutaneous catheters and tubes and as an adjunct to hemostasis in sealing residual oozing of tissue tracts of femoral access sites that have been previously closed by suture/collagen-based hemostatic devices.

In addition, D-Stat is legally marketed internationally in the following countries: Austria, Belgium, Denmark, Germany, Greece, Ireland, Israel, Italy, Portugal, South Africa, Spain, Sweden, Switzerland, the Netherlands, and the United Kingdom.

D-Stat has not been withdrawn from the market in any country for any reason related to the safety or effectiveness of the device.

VIII. Potential Adverse Effects of the Device on Health

The study's primary safety endpoint, defined as study-related major adverse events, was designed to test non-inferiority of treatment to control. The results, presented in **Table 8** of section X, "Summary of Clinical Study", by type of adverse event, show that the investigational group yielded a major study-related

adverse event rate of 21.3% (29/136) compared to the control group at 27.8% (37/133). The corresponding p-value for non-inferiority was 0.0008, below the a priori alpha level of 0.05, demonstrating non-inferiority of treatment to control for this endpoint.

Descriptive data that characterizes additional safety findings are provided for study related minor complications. These results are summarized in **Table 10** of section X, "Summary of Clinical Study". No statistically significant differences were observed between the study groups, as evidenced in a study related minor complication rate of 5.1% (7/136) in the investigation group versus 3.0% (4/133) in the control group. (p=0.54, Fisher's exact test).

A total of 12 study subjects expired during the conduct of this investigation. No deaths were determined attributable to use of the D-Stat Flowable Hemostat. A summary of the conditions associated with these deaths are provided in **Table 11** of section X, "Summary of Clinical Study".

IX. Summary of Preclinical Studies

Please refer to P990037 original submission for a summary of preclinical studies.

X. Summary of Clinical Study

A. Study Design

D-Stat Flowable Hemostat was evaluated in the prepectoral pocket application through conduct of the "Pocket Protector" clinical investigation. The "Pocket Protector" study was a controlled, prospective, randomized, multi-center trial that evaluated the safety and effectiveness of D-Stat Flowable Hemostat in an anti-coagulated patient population undergoing new placement of a pulse generator (e.g., pacemaker or ICD).

The primary safety objective, designed for non-inferiority, was to demonstrate a similar rate of study related major adverse events between the study treatment groups. The primary effectiveness objective, designed for superiority, was to demonstrate a statistically significant reduced incidence rate of clinically relevant prepectoral pocket hematoma formation in the investigation group when compared to the control group. Secondary objectives consisted of evaluation for minor adverse events (safety) and duration of procedure, time to discharge and patient satisfaction (effectiveness).

The randomization schedule was two-celled and stratified by pulse generator type (pacemaker vs. ICD) to ensure adequate representation of the ICD population

with a minimum of 40% ICDs being implanted. Study subjects were evaluated pre-procedure, through discharge, at 15-days and 8-weeks.

A total of 269 subjects (133 control, 136 investigation) were enrolled. The control population was comprised of patients that received the standard of care for achieving hemostasis in the prepectoral pocket (i.e., standard compression, electrocautery, and/or untreated cotton pledgets). The investigation population was comprised of patients that received the aforementioned standard of care and D-Stat Flowable. Overall pulse generator distribution rates are representative of 54.6% pacemakers and 45.4% ICDs. Study treatment group pacemaker/ICD ratios were 54.4% pacemakers and 45.6% ICDs for the investigation group with a similar distribution observed in the control group of 54.9% pacemakers and 45.1% ICDs. Refer to **Table 1** for greater detail.

Table 1: Distribution Ratio of Pulse Generator Type by Treatment Groups

Pulse Generator Type	Investigation Group n = 136		Control Group n = 133		Combined Group n = 269	
	x	%	x	%	x	%
Pacemaker	74	54.4	73	54.9	147	54.6
ICD	62	45.6	60	45.1	122	45.4
Total:	136	100.0	133	100.0	269	100.0

B. Patient Selection Criteria

Inclusion Criteria

The inclusion criteria established for this investigation are:

- Patients 18 years of age or older.
- Patients undergoing a prepectoral implant procedure for new placement of a pacemaker or implantable cardioverter defibrillator.
- Patients receiving anticoagulation therapy (i.e., Heparin, LMWH, Coumadin/Warfarin, or Plavix) and require timely resumption (<24 hours) of the anticoagulation therapy post-procedure.
- Coumadin patients with a documented baseline INR that is ≤ 2.0.
- Patients willing and able to comply with the requirements of the study protocol, including the predefined follow-up evaluations.
- Patients who are willing and able to provide appropriate written informed consent.

Exclusion Criteria

The exclusion criteria established for this investigation are:

- Coumadin patients who have a documented baseline INR that is > 2.0.
- Patients whose anti-coagulation therapy regime does not include pre-procedure Heparin, LMWH, Coumadin/Warfarin, or Plavix administration and/or timely resumption (>2 4 hours) of anticoagulation therapy after the implantation procedure.
- Patients who have received thrombolytic therapy (e.g., streptokinase, urokinase, t-PT) in the preceding 24 hours.
- Patients presenting for revision of a pacemaker or implantable cardioverter defibrillator procedure.
- Patients who are known or suspected to be lactating or pregnant (requires documentation of negative pregnancy testing result in women of childbearing age [18 – 44] or potential).
- Patients with known allergies to bovine derived products.
- Patients with a previous exposure to injectable collagen implants.
- Patients with a know history of bleeding disorders (i.e, thrombocytopenia [platelets < 100,000], thrombasthenia, hemophilia, or Von Willebrand's disease).
- Patients that are concurrently participating in an investigational study that may confound the treatment or outcomes of the present study.
- Patients with an active infection at the implant site.
- Patient in whom absorbable hemostatic agents are contraindicated.

C. Clinical Study Results

1. Patient Population

The first study subject was enrolled on June 12, 2003. Ten (10) U.S. investigative sites utilizing institutions governed by eleven (11) Institutional Review Boards (IRBs), as a single site contributed patients at two (2) hospitals with separate governing IRBs, provided data for this clinical report. Subjects underwent new placement of a pulse generator (e.g., pacemaker or ICD) in the prepectoral pocket. In addition, entrance criteria required that one or more of the following anti-clotting therapy agents be resumed within 24-hours post-procedure: Heparin, LMWH, Coumadin, and/or Plavix.

2. Baseline Demographic Data

The patient population for this trial was homogenous across study treatment groups as demonstrated in the baseline demographic data summarized in **Table 2 through Table 7**. Similar baseline characteristic distributions were observed between the control and investigation groups across all parameters. Further no statistically significant differences were observed. **Table 2** presents the gender distribution by treatment group and for the overall study population.

Table 2: Gender Distribution by Treatment Group

Gender	Investigation Group n = 136		Control Group n = 133		p-value*	Combined Treatment Group	
	x	%	x	%		x	%
Male	89	65.4	95	71.4	0.298	184	68.4
Female	47	34.6	38	28.6		85	31.6
Total:	136	100.0	133	100.0		269	100.0

*Fisher's Exact Test, 2-sided

Table 3 presents mean baseline physical characteristics by treatment group and for the combined study population.

Table 3: Comparison of Mean Baseline Physical Characteristics by Treatment Group

Physical Characteristic	n	Mean	Standard Deviation	Standard Error Mean	p - value
Age					
Investigation	136	73.27	11.44656	0.98153	0.49
Control	133	72.21	13.44864	1.16614	
Weight (kg)					
Investigation	136	78.19	16.00253	1.37221	0.48
Control	133	79.6	18.72662	1.62380	
Height (cm)					
Investigation	136	170.07	10.66481	0.91450	0.83
Control	132	170.38	12.38671	1.07812	
Body Mass Index (BMI)					
Investigation	136	27.01	4.84696	0.41562	0.52
Control	132	27.45	6.31990	0.55008	
Heart Rate					
Investigation	136	74.79	19.471	1.670	0.41
Control	132	72.87	18.358	1.598	
Blood Pressure (systolic)					
Investigation	136	138.76	27.323	2.343	0.43
Control	132	136.11	27.392	2.384	
Hemoglobin Lab Test					
Investigation	134	12.88	1.9147	0.1654	0.68
Control	133	12.98	1.8758	0.1627	
Hematocrit Lab Test					
Investigation	134	38.43	5.5840	0.4824	0.77
Control	133	38.62	5.4265	0.4705	

Table 4 presents the combined study population conduction disorders by treatment group.

Table 4: Main Conduction Disorder Distribution by Treatment Group

Conduction Disorder	Investigation Group n = 136		Control Group n = 133		Combined Group n = 269	
	x	%	x	%	x	%
Atrial Fibrillation/Flutter	33	24.3	27	20.3	60	22.3
Bradycardia	24	17.6	17	12.8	41	15.2
Complete AV Block	9	6.6	6	4.5	15	5.6
Complex Ventricular Ectopy	7	5.1	10	7.5	17	6.3
Prophylactic	27	19.9	30	22.6	57	21.2
Second Degree AV Block	2	1.5	4	3.0	6	2.2
Sick Sinus Syndrome	11	8.1	15	11.3	26	9.7
Other	23	16.9	24	18.0	47	17.5
Total:	136	100.0	133	100.0	269	100.0

Table 5 presents the combined study population underlying diagnosis by treatment group.

Table 5: Main Diagnosis Distribution by Treatment Group

Main Underlying Diagnosis	Investigation Group n = 136		Control Group n = 133		Combined Group n = 269	
	x	%	x	%	x	%
Aborted Sudden Cardiac Death	2	0.7	2	0.7	4	1.4
Cardiomyopathy	34	12.6	28	10.4	62	23
Congenital Heart Disease	-	-	1	0.4	1	0.4
Congestive Heart Failure	22	8.2	14	5.2	36	13.4
Coronary Artery Disease	26	9.7	30	11.2	56	20.9
Following Acute Phase of MI	1	0.4	0	0.0	1	0.4
Myocardial Ischemia or Infarction	3	1.1	4	1.5	7	2.6
Primary Electrical Disease	16	6.0	16	5.9	32	11.9
Syncope or Pre-Syncope	22	8.2	27	10.0	49	18.2
Other	10	3.7	11	4.1	21	7.8
Total:	136	50.6	133	49.9	269	100.0

A comparison of baseline cardiac risk factors by treatment group and for the overall study population is presented in **Table 6**.

Table 6: Comparison of Baseline Risk Factors by Category and Treatment Group

Medication Type	Investigation Group n = 136		Control Group n = 133		p-value*	Combined Group n = 269	
	x	%	x	%		x	%
Tobacco Use							
Yes	64	47.1	64	48.1	0.903	128	47.6
No	72	52.9	69	51.9		141	52.4
Total	136	100.0	133	100.0		269	100.0
	(n = 64)		(n – 64)			(n = 128)	
Current Tobacco Use	17	26.6	18	28.1	1.000	35	27.3
Remote Tobacco Use	48	75.0	48	76.2	1.000	96	75.6
Diabetes Mellitus							
Yes	40	29.4	38	28.6	0.894	78	29.0
No	96	70.6	95	71.4		191	71.0
Total	136	100.0	133	100.0		269	100.0
	(n = 40)		(n = 38)			(n = 78)	
Controlled on Oral Meds[1]	27	67.5	20	52.6	0.248	47	60.3
Controlled on Insulin[1]	14	35.0	18	47.4	0.358	32	41.0
History of CVA / TIA							
Yes	26	19.1	23	17.3	0.753	49	18.2
No	110	80.9	110	82.7		220	81.8
Total	136	100.0	133	100.0		269	100.0
History of MI							
Yes	53	39.0	54	40.6	0.804	107	39.8
No	83	61.0	79	59.4		162	60.2
Total	136	100.0	133	100.0		269	100.0
History of PVD / Claudication							
Yes	19	14.0	17	12.8	0.858	36	13.4
No	117	86.0	116	87.2		233	86.6
Total	136	100.0	133	100.0		269	100.0
Hyperlipidemia Requiring Meds							

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Yes	88	64.7	89	66.9	0.797	177	65.8
No	48	35.3	44	33.1		92	34.2
Total	136	100.0	133	100.0		269	100.0
Hypertension Requiring Meds							
Yes	106	77.9	99	74.4	0.567	205	76.2
No	30	22.1	34	25.6		64	23.8
Total	136	100.0	133	100.0		269	100.0
"Other"							
Yes	97	71.9	98	74.2	0.681	195	73.0
No	38	28.1	34	25.8		72	27.0
Total	135	100.0	132	100.0		267	100.0

* Fisher's Exact Test, 2-sided

[1] 2 study subjects with diabetes mellitus were controlled on diet alone and 3 subjects with diabetes mellitus required both insulin and oral medication to manage their diabetic condition.

Table 7 compares baseline medication administration between treatment groups and for the overall study population.

Table 7: Comparison of Baseline Medication Administration by Category and Treatment Group

Medication Type	Investigation Group n = 136		Control Group n = 133		p-value*	Combined Group n = 269	
	x	%	x	%		x	%
Anti-Coagulant							
Yes	113	83.1	100	75.2	0.133	213	79.2
No	23	16.9	33	24.8		56	20.8
Total	136	100.0	133	100.0		269	100.0
Oral Anti-Platelet or Platelet Inhibitor							
Yes	90	66.2	92	69.2	0.605	182	67.7
No	46	33.8	41	30.8		87	32.3
Total	136	100.0	133	100.0		269	100.0
GP IIB/IIIA Platelet Inhibitor							
Yes	2	1.5	4	3.0	0.444	6	2.2
No	134	98.5	129	97.0		263	97.8
Total	136	100.0	133	100.0		269	100.0
Thrombin Inhibitor							
Yes	1	0.7	0	0.0	1.000	1	0.4
No	135	99.3	133	100.0		268	99.6
Total	136	100.0	133	100.0		269	100.0
"Other"							
Yes	0	0.0	0	0.0	1.000	0	0.0
No	136	100.0	133	100.0		269	100.0
Total	136	100.0	133	100.0		269	100.0

*Fisher's Exact Test, 2-sided

3. *Primary Safety Endpoint Results*

The study's primary safety endpoint, defined as study-related major adverse events, was designed to test non-inferiority of treatment to control. The results, presented in **Table 8** by type of adverse event, show that the investigational group yielded a major study-related adverse event rate of 21.3% (29/136) compared to the control group at 27.8% (37/133). The corresponding p-value for non-inferiority was 0.0008, below the a priori alpha level of 0.05, demonstrating non-inferiority of treatment to control for this endpoint.

Table 8: Subjects Experiencing Major Study-Related Adverse Events By Type

Event Type	Investigational Group (n=136)		Control Group (n=133)		Combined Groups (n=269)	
	N	%	N	%	N	%
Pocket Related Subtotal	**18**	**13.2%**	**33**	**24.8%**	**51**	**19.0%**
Hematoma	15	11.0%	27	20.3%	42	15.6%
Infection	1	0.7%	5	3.8%	6	2.2%
Wound dehiscence	1	0.7%	0	0.0%	1	0.4%
Drainage from site	0	0.0%	1	0.8%	1	0.4%
Swelling	2	1.5%	0	0.0%	2	0.7%
Lead Related Subtotal	**5**	**3.7%**	**1**	**0.8%**	**6**	**2.2%**
Dislodgement	4	2.9%	0	0.0%	4	1.5%
Lead perforation of the cardiac chamber	0	0.0%	1	0.8%	1	0.4%
Difficulty with lead	1	0.7%	0	0.0%	1	0.4%
Venous Access Related Subtotal	**4**	**2.9%**	**2**	**1.5%**	**6**	**2.2%**
Pneumothorax	4	2.9%	2	1.5%	6	2.2%
Device Related Subtotal	**2**	**1.5%**	**0**	**0.0%**	**2**	**0.7%**
High DFTs	1	0.7%	0	0.0%	1	0.4%

Subject received shock	1	0.7%	0	0.0%	1	0.4%
Other Related Subtotal	**0**	**0.0%**	**1**	**0.8%**	**1**	**0.4%**
Hypotension	0	0.0%	1	0.8%	1	0.4%
Other Events Subtotal	**1**	**0.7%**	**2**	**1.5%**	**3**	**1.1%**
Total	**29**	**21.3%**	**37**	**27.8%**	**67**	**24.9%**

Note: columns may not sum since subjects may have had AEs in multiple categories.

4. Primary Effectiveness Endpoint Results

Primary effectiveness was expressed as a statistically significant difference in the rate of clinically relevant hematoma formation within the prepectoral pocket following implantation of a pulse generator. Clinical relevance of hematoma formation, defined as alteration in the standard of care (i.e., application of a compression bandage, alteration of their anti-clotting regime [Heparin, LMWH, Coumadin or Plavix] or evacuation of the hematoma) was determined by an independent Clinical Events Committee (CEC). The CEC, blinded to both the treatment group and the treatment administered by the study investigator for the hematoma, adjudicated all hematomas reported in the trial.

Within this investigation, the primary effectiveness endpoint was successfully demonstrated. The investigation group yielded a clinically relevant hematoma rate of 11.76% (16/136) compared to the control group with a clinically relevant hematoma rate of 22.56% (30/133). The difference between the two groups is statistically significant (p = 0.0231). Further, this difference translates to a 48% reduction of clinically relevant hematomas observed in the investigation group.

Table 9: Incidence Rates of Clinically Relevant Hematomas

Generator Type	Investigation Group			Control Group			p-value*	95% Confidence Interval (CI)
	%	x	n	%	x	n		
All Generator Types	11.76	16	136	22.56	30	133	0.0231	1.37%, 20.03%
Pacemakers	8.11	6	74	20.55	15	73	0.0358	0.75%, 24.41%
ICDs	16.13	10	62	25.00	15	60	0.2659	-5.74%, 23.59%

*p-values from Fisher's exact test.

5. Secondary Safety Objective Results

Descriptive data that characterizes additional safety findings are provided for study related minor complications. These results are summarized in **Table 10**.

Table 10: Subjects Experiencing Minor Study Related Adverse Events

Event Type	Investigational Group (n=136)		Control Group (n=133)		Combined Groups (n=269)	
	N	%	N	%	N	%
Pocket Related (Subtotal)	**0**	**0.0%**	**1**	**0.8%**	**1**	**0.4%**
Hematoma with bleeding	0	0.0%	1	0.8%	1	0.4%
Lead Related (Subtotal)	**3**	**2.2%**	**0**	**0.0%**	**3**	**1.1%**
Dislodgement	1	0.7%	0	0.0%	1	0.4%
Malposition	1	0.7%	0	0.0%	1	0.4%
Lead Malposition	1	0.7%	0	0.0%	1	0.4%
Venous Access Related (Subtotal)	**3**	**2.2%**	**0**	**0.0%**	**3**	**1.1%**
Pneumothorax	3	2.2%	0	0.0%	3	1.1%
Device Related (Subtotal)	**1**	**0.7%**	**0**	**0.0%**	**1**	**0.4%**
Elevated LV Threshold	1	0.7%	0	0.0%	1	0.4%
Other Events (Subtotal)	**0**	**0.0%**	**3**	**2.3%**	**3**	**1.1%**
Total	**7**	**5.1%**	**4**	**3.0%**	**11**	**4.1%**

Note: columns may not sum since subjects may have had AEs in multiple categories.

No statistically significant differences were observed between the study groups, as evidenced in a study related minor complication rate of 5.1% (7/136) in the investigation group versus 3.0% (4/133) in the control group. (p=0.54, Fisher's exact test).

6. Reported Deaths

A total of 12 study subjects expired during the conduct of this investigation. No deaths were determined attributable to use of the D-Stat Flowable Hemostat.

A summary of the conditions associated with these deaths are provided in **Table 11**.

Table 11: Deaths reported during trial

Event	Investigation n = 136		Control n = 133	
	x	%	x	%
Pulmonary Embolis	0	0	1	0.8
End stage Congestive Heart Failure	1	0.7	0	0
Cause Unknown*	1	0.7	0	0
Renal Failure	0	0	2	1.5
Refractory Endocarditis	0	0	1	0.8
Pneumonia	1	0.7	-	-
Cardiac/Cardiopulmonary Arrest	0	0	2	1.5
Multi-factorial Generalized Deterioration	1	0.7	0	0
Lead Perforation of Cardiac Chamber	0	0	1	0.8
Irreversible Ventricular Tachycardia	0	0	1	0.8
Total:	4	2.9	8	6.0

*The cause of death is unknown. Multiple attempts by the investigative site to discover the cause of death were unsuccessful.

7. *Secondary Effectiveness Objective Results*

Beyond supporting the primary effectiveness endpoint, this investigation evaluated secondary effectiveness parameters that include Duration of Procedure (incision to closure), Time to Discharge (procedure end to time eligible for discharge) and Patient Satisfaction (modified Odom's Criteria). Analyses of these data points revealed similar results between groups without observance of statistical differences. These findings are summarized in **Table 12** through **Table 14**.

Table 12 presents the mean duration of procedure by treatment group and for the combined overall study population.

Table 12: Mean Procedure Duration

Treatment Group	n	Mean Procedure Time (Minutes)	Standard Deviation	Standard Error Mean	p-value*
D-Stat	136	61.0735	79.07368	6.78051	0.214
Control	132	51.4545	40.71974	3.54420	

*Student's T-Test, 2-sided

Table 13 presents the mean time to discharge by treatment group and for the overall combined study population.

Table 13: Mean Time to Discharge

Treatment Group	n	Mean Time to Discharge (Hours)	Standard Deviation	Median Time to Dischard	p-value*
D-Stat	135	61.0	99.4	25.9	0.352
Control	128	45.8	46.5	24.3	

*Student's T-Test, 2-sided

Table 14 presents patient satisfaction by treatment group and for the overall combined study population. For analysis purposes the classifications have been collapsed to represent Excellent/Good and Fair/Poor responses.

Table 14 Comparison of Patient Satisfaction by Treatment Group

Level of Subject Satisfaction by Interval	Investigation		Control		Combined Groups	
	x	%	x	%	x	%
24-Hour						
Excellent	25	27.2	32	33.7	57	30.5
Good	34	37.0	27	28.4	61	32.6
Fair	6	6.5	7	7.4	13	7.0
Poor	0	0	0	0	0	0
Not Rated	27	29.3	29	30.5	56	29.9
Total	92	100.0	95	100.0	187	100.0
Other						
Excellent	35	34.0	27	29.7	62	32.0
Good	55	53.4	52	51.7	107	55.2
Fair	8	7.8	6	6.6	14	7.2
Poor	1	1.0	1	1.1	2	1.0
Not Rated	4	3.9	5	5.5	9	4.6
Total	103	100.0	91	100.0	194	100.0
15-Day						
Excellent	64	47.8	59	46.1	123	46.9
Good	60	44.8	55	43.0	115	43.9
Fair	8	6.0	13	10.2	21	8.0
Poor	0	0	0	0	0	0
	2	1.5	1	0.8	3	1.1
Total	134	100.0	128	100.0	262	100.0
8-Week						
Excellent	90	69.2	76	61.8	166	65.6
Good	35	26.9	38	30.9	73	28.9
Fair	3	2.3	3	2.4	6	2.4
Poor	0	0	1	0.8	1	0.4
Not Rated	2	1.5	5	4.1	7	2.8
Total	130	100.0	123	100.0	253	100.0

D. Conclusions Drawn From the Clinical Study

The results of this clinical investigation provide reasonable assurance that use of D-Stat Flowable Hemostat in the prepectoral pocket during implantation of a pulse generator is safe and effective for the intended population. This conclusion is evidenced in:

- A similar rate of study related major adverse events observed between treatment groups (p=0.025)
- A statistically significant difference (p = 0.0231) in the incidence rate of clinically relevant hematomas observed in the investigation group (11.76%; 16/136) when compared to the control group (22.56%; 30/133).
- An overall 48% reduction in the occurrence of clinically relevant hematomas for patients treated with the D-Stat Flowable Hemostat.

XI. Conclusions Drawn from Studies

Results of the studies provide valid scientific evidence and reasonable assurance that the D-Stat Flowable Hemostat is safe and effective when used in accordance with its Instructions for Use.

XII. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by the panel.

XIII. CDRH Decision

FDA issued an approval order on December 22, 2006.

XIV. Approval Specifications

Directions for Use:	See labeling.
Hazards for Health from Use of the Device:	See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the labeling.
Postapproval Requirements and Restrictions:	See approval order.